Notice of Allowability	Application No.	Applicant(s)	
	10/033,297	HALL ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *8/9/2007*.

2. ☒ The allowed claim(s) is/are *35,47,62-66,68-75 and 77-84*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *10/2007* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Reasons for Allowance

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ms. Mary Ann Brow (Reg. No. 42,363) on October 25, 2007.

2. The application has been amended as follows:

Rejoin claims 64, 69, 70, 74, 75, and 77 with claims 35, 47, 62, 63, 65, 66, 68, 71-73, and 78-84.

35. (Currently amended) A method of detecting a target polynucleotide which comprises the steps of:

a) contacting a target polynucleotide having a first portion and a second portion immediately contiguous to one another with:

i) an invader oligonucleotide, at least a part of which is capable of specifically hybridizing to the first portion of the target polynucleotide;

ii) a first probe oligonucleotide comprising a first region that is capable of specifically hybridizing to the second portion of the target polynucleotide and an unpaired region located adjacent to the first region; and

iii) a reagent that is capable of cleaving to release the unpaired region of the first probe oligonucleotide to produce a cleaved unpaired region [to form a first cleavage structure], wherein said reagent comprises a 5' nuclease;

producing said cleaved unpaired region by cleaving said first probe oligonucleotide, forming a [second] cleavage structure[-]comprising said cleaved unpaired region and a second probe oligonucleotide by hybridizing said cleaved unpaired region to said second probe oligonucleotide, or forming a cleavage structure comprising said cleaved unpaired region, said second probe oligonucleotide, and a target nucleic acid by hybridizing said cleaved unpaired region and said second probe oligonucleotide to [a] said [second] target [polynucleotide] nucleic acid, and generating a cleaved second probe by cleaving said second cleavage structure using the reagent;

b) detecting the accumulation of the cleaved second probe oligonucleotide; and

c) determining whether the cleaved second probe oligonucleotide accumulates exponentially over time, wherein said exponential accumulation of the cleaved second probe oligonucleotide over time is indicative of the presence of said target [nucleic acid] polynucleotide.

47. (Currently amended) The method of Claim 35 wherein said detecting the accumulation of the cleaved second probe oligonucleotide comprises detection of fluorescence or phosphorescence.

62. (Currently amended) A method for detecting the presence of a first target nucleic acid [molecule] in a sample, comprising:

a) incubating a sample containing a first target nucleic acid with [a cleavage agent,] a first nucleic acid molecule and a second nucleic acid molecule and forming a first cleavage structure, said first cleavage structure comprising:

i) said first target nucleic acid comprising a first region and a second region, said second region upstream of and contiguous to said first region;

ii) said first nucleic acid molecule comprising a first portion that is completely complementary the second region of the first target nucleic acid;

iii) said second nucleic acid molecule comprising a 3' portion and a 5' portion, wherein said 5' portion is completely complementary to said first region of said first target nucleic acid;

wherein said 5' portion of said second nucleic acid molecule is annealed to said first region of said first target nucleic acid and wherein at least a portion of said first nucleic acid molecule is annealed to said second region of said first target nucleic acid, and wherein [said first nucleic acid molecule comprises] a 5' portion <u>of said first nucleic acid molecule</u> [that] is not annealed to said <u>first</u> target nucleic acid,

b) cleaving said first cleavage structure with a cleavage agent comprising a 5' nuclease, generating <u>a</u> non-target cleavage product, and forming a second cleavage structure comprising:

i) said non-target cleavage product; and

ii) a probe oligonucleotide;

by hybridizing said non-target cleavage product to said probe oligonucleotide, or <u>forming a second cleavage structure comprising:</u>

i) said non-target cleavage product;

ii) said probe oligonucleotide; and

iii) a second target nucleic acid;

by hybridizing both said non-target cleavage product and said probe oligonucleotide to [a] said second target nucleic acid, and

c) cleaving said second cleavage structure with said cleavage agent, generating a cleaved probe and detecting said cleaved probe at a plurality of time points, wherein said cleaved probe accumulates at an exponential rate over time, and wherein the accumulation of said cleaved probe at an exponential rate over time indicates the presence of said first target nucleic acid in said sample[; and

d) detecting said cleaved probe at a plurality of timepoints].

68. (Currently amended) The method of Claim 62, wherein said 5' nuclease is a thermostable 5' nuclease.

69. (Currently amended) The method of Claim 68, wherein said thermostable 5'nuclease [comprises] is a 5' nuclease of a DNA polymerase.

72. (Currently amended) The method of Claim 71, wherein said single nucleotide is complementary to said first target nucleic acid.

73. (Currently amended) The method of Claim 62[, wherein] further comprising providing a plurality of said first nucleic acid molecule [is provided,] such that said first nucleic acid molecule is in concentration excess compared to said first target nucleic acid.

74. (Currently amended) The method of Claim 62[, wherein] further comprising providing a plurality of said second nucleic acid molecule [is provided,] such that said second nucleic acid molecule is in concentration excess compared to said first target nucleic acid.

75. (Currently amended) The method of Claim 62, wherein said first target nucleic acid and said second nucleic acid molecule form a duplex, and [wherein] further comprising providing a plurality of said first nucleic acid molecule [is provided] such that said first nucleic acid molecule is in concentration excess compared to said duplex.

77. (Currently amended) The method of Claim 75, wherein said non-target cleavage product is generated from said first nucleic acid molecule and is [generated] in concentration excess compared to said duplex.

81. (Currently amended) The method of Claim 35, wherein said [reagent] 5' nuclease is a thermostable 5'nuclease.

3. The following is an examiner's statement of reasons for allowance:

Claims 35, 47, 62-66, 68-75, and 77-84 are allowable in light of applicant's amendments filed on August 9, 2007, terminal disclaimers filed on August 9, 2007, December 22, 2006, and September 18, 2006, and the examiner's amendments. The rejections under 35 U.S.C 112, second paragraph have been withdrawn in view of the applicant's amendments filed on August 9, 2007 and the examiner's amendments. The closest prior art in the record is Goodman *et al.*, (US Patent No. 4,994,368, published on February 19, 1991). This prior art does not teach that said reagent comprises a 5' nuclease and producing step in claim 35 and step (b) of claim 62. This prior art either alone or in combination with the other art in the record does not teach or reasonably suggest a method of detecting a target polynucleotide and a method for detecting the

presence of a first target nucleic acid in a sample which comprise all of the limitations recited in claims 35 and 62.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

October 25, 2007

FRANK LU
PRIMARY EXAMINER